

REMARKS

Claims 1-3, 7-9, 11, and 13-18 have been amended, as set forth above, to correct an informality. Specifically, claims 1-3, 7-9, 11, and 13-18 have been amended to add the article "an" before " α -hydroxycarboxylic acid." Claim 17 has been amended to recite a hydrocarbon solvent "selected from chain hydrocarbons containing 5 to 16 carbons, saturated monocyclic hydrocarbons containing between 6 and 16 carbon atoms, and aromatic hydrocarbons." Support for the amendment to claim 17 can be found throughout the specification, for example, at page 17, third paragraph, through page 18, fourth paragraph. Claim 19 has been amended. Support for the amendment to claim 19 can be found, for example, at page 46, first paragraph.

Accordingly, the amendments add no new matter. With entry of the Amendment, claims 1-3, 7-9, 11, and 13-19 are pending.

Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 1-3, 7-9, 11, and 13-19 under 35 U.S.C. § 112, first paragraph, alleging that "the specification, while being enabling for α -hydroxycarboxylic acid, such as chloromandelic acid, mandelic acid, does not reasonably provide enablement for all the α -hydroxycarboxylic acids known in the field of chemistry." *Action* at page 2. Applicants respectfully traverse.

The Examiner's rejection continues, "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to include all the α -hydroxycarboxylic acids known in chemistry." *Action* at page 2. However, the rejection does not identify which aspect of the method claims allegedly lack enablement. Applicants specify a substrate (cyanohydrin), a reaction (hydrolysis) and a solvent, but the Examiner has not indicated which aspects are not enabled. The Examiner only asserts that not "all α -hydroxycarboxylic

acids” are enabled. The application enables all those α -hydroxycarboxylic acids that can be produced using the recited methods.

Indeed, the rejection reads as though Applicants claimed α -hydroxycarboxylic acids as compositions. However, as noted above, claims 1-3, 7-9, 11, and 13-18 recite methods. Each step of those claimed methods is fully enabled by the specification. For example, claim 1 recites, a “method for producing an α -hydroxycarboxylic acid, which comprises hydrolyzing cyanohydrin in the presence of a hydrocarbon solvent selected from chain hydrocarbons containing 5 to 16 carbons, saturated monocyclic hydrocarbons containing between 6 and 16 carbon atoms, and aromatic hydrocarbons” That claim comprises a single step, which is discussed throughout the specification, including in the two examples. *See e.g., Specification*, at page 47, through page 54. Applicants respectfully request that the Examiner reconsider and withdraw the rejection, or more clearly articulate what step in that method is not enabled.

Claim 19 was also rejected for allegedly not being enabled “for all the α -hydroxycarboxylic acids known in the field of chemistry.” However, that claim does not recite “ α -hydroxycarboxylic acids.” Rather, claim 19 recites an “optically active chloromandelic acid.” Applicants respectfully request a withdrawal of this rejection.

The Examiner rejected claims 1, 7, 17, and 18 under 35 U.S.C. § 112, first paragraph, alleging that “the specification, while enabling for cyanohydrin, such as mandelonitrile (2-hydroxy-2-phenylacetone nitrile), 3-phenoxymandelonitrile, (2-hydroxy-2-(3-phenoxyphenyl)acetone nitrile), and etc., does not reasonably provide enablement for all the cyanohydrins known in the field of chemistry.” *Action* at page 2. This rejection suffers from the same deficiencies discussed above. It fails to identify a step in any of the claimed methods that is not enabled. Furthermore, the specification provides extensive guidance to one skilled in the

art in selecting a cyanohydrin. For example, the specification discusses a cyanohydrin as follows:

In the first aspect of the invention, cyanohydrin used as a material for the present invention is not particularly limited, as long as it has, in a molecule thereof, at least one pair consisting of a hydroxyl group and a cyano group which bind to an identical carbon atom.

Specification, at page 6. The specification then provides structure for cyanohydrins and goes on to provide examples of certain cyanohydrins for the following *ten* pages. See *Specification* at pages 6-16.

Finally, as to both of the rejections under 35 U.S.C. § 112, first paragraph, the Examiner asserts that the specification adequately enables the claimed methods using certain cyanohydrins and resulting in certain α -hydroxycarboxylic acids, but fails to enable the claimed methods using any cyanohydrin to produce any corresponding α -hydroxycarboxylic acid. This is not a proper basis for a rejection of these claims. There can be no doubt that the specification enables one of ordinary skill in the art to perform the steps of any of the claimed methods using any cyanohydrin. Importantly, even if such methods using certain cyanohydrins fail to produce an α -hydroxycarboxylic acid, the enablement requirement of § 112, first paragraph, is still satisfied.

“The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled.” *Manual of Patent Examining Procedure* § 2164.08(b) (8th ed. 2001) (“MPEP”). The standard is whether a skilled artisan “could determine which embodiments that were conceived, but not yet made, would be inoperative with expenditure of no more effort than is normally required in the art.” *Id.* It is well within ordinary skill in the art to perform the claimed methods and then determine the presences of the desired α -hydroxycarboxylic acid using routine well-established methods. For example, the specification

discusses making such determination by "HPLC." *See, e.g., Specification* at page 50. HPLC (high performance liquid chromatography) was well known to one skilled in the art at the time the present application was filed. *See, e.g., Robert D. Braun, Introduction to Instrumental Analysis*, McGraw-Hill, Inc., pages 839-840 (1987) (copy enclosed). Pursuant to the provision of § 609 III(C)(3) of the MPEP, Applicants submit, herewith, a PTO Form 1449 listing that document. *See MPEP* at page 600-132. Applicants respectfully request that the Examiner consider that document and indicate that it was considered by making the appropriate notation on the attached form.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claim 17 alleging that the term "hydrocarbon solvent" is "vague and indefinite." *Action* at page 3. Solely to expedite prosecution and without acquiescing to any of the Examiner's contentions, claim 17 has been amended to recite a hydrocarbon solvent "selected from chain hydrocarbons containing 5 to 16 carbons, saturated monocyclic hydrocarbons containing between 6 and 16 carbon atoms, and aromatic hydrocarbons." Thus the rejection is moot.

Rejection Under 35 U.S.C. § 102

The Examiner rejected claims 1-3, 7-9, 11, 13, 14, 17, and 18, under 35 U.S.C. § 102 for allegedly being anticipated by Effenberger et al (Tetrahedron Letters p. 2608) (hereinafter "Effenberger"). *Action* at page 3. Applicants traverse.

For a reference to anticipate the claimed invention under 35 U.S.C. § 102, the reference must describe the invention such that "each and every limitation is found either expressly or

inherently" within it. *Transclean Corp. v. Bridgewood Services, Inc.*, 290 F.3d 1364, 1370, 62 USPQ2d 1865, 1869 (Fed. Cir. 2002) (citations omitted); *see* MPEP § 2131 (8th ed. 2001) ("to anticipate a claim, the reference must teach every element of the claim"). Effenberger does not teach all of the elements of the rejected claims. For example, Effenberger does not discuss hydrolyzing cyanohydrin in the presence of a hydrocarbon solvent, as recited in the rejected claims. Although Effenberger discusses a hydrolysis reaction and subsequent crystallization from n-hexane, the n-hexane is not present in the hydrolyzation reaction. *See Effenberger* at p. 2608, n. 15.

Thus, for at least that reason, Effenberger cannot anticipate claims 1-3, 7-9, 11, 13, 14, 17, and 18.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) in view of Effenberger.

Rejection under 35 U.S.C. § 103

The Examiner rejected claims 15 and 16 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Effenberger in view of Kawabe. *See Action* at page 5. Each of those claims depends from claim 1, which the Examiner alleged was anticipated by Effenberger. The Examiner cited Kawabe as allegedly showing certain additional elements of dependant claims 15 and 16.

For at least the reason stated above, Effenberger does not anticipate claim 1. Further, the Applicants note that, in making the rejection under § 103, the Examiner mischaracterized Effenberger. The examiner stated that "Effenberger et al expressly teaches the method of producing (R)- α -hydroxy- α -methyl-heptanoic acid by hydrolyzing a (R)- α -hydroxy- α -methyl heptane nitrile in the presence of hydrochloric acid and the hexane solvent." *Action* at page 6.

As discussed above, in Effenberger, the n-hexane is not present in the hydrolyzation reaction. Accordingly, Effenberger cannot anticipate the claim 1, from which claims 15 and 16 depend.

Moreover, Kawabe does not remedy the deficiencies of Effenberger. Contrary to the Examiner's contention, Kawabe does not discuss a method of hydrolyzing cyanohydrin in the presence of a hydrocarbon solvent, such as hexane, benzene, or xylene. *See Action* at page 6.

The Examiner alleged that:

Kawabe et al teaches a process for producing a carboxylic acid by hydrolyzing a nitrile compound (see col. 1, lines 13-15), such as an alpha-cyanohydrin (see col. 5, lines 31-50), in the presence of an acidic catalyst and a hydrocarbon solvent, such as hexane, benzene, or xylene (see col. 14, lines 21-44).

Id. The Examiner is mistaken. The last citation (col. 14, lines 21-44) discusses a hydrocarbon solvent, but that discussion is in the context of an amide extracting step, not a hydrolyzing step. *See Kawabe* col. 13, line 31 through col. 14, line 45. Accordingly, that section cannot support the Examiner's contention that Kawabe teaches hydrolyzing in the presence of a hydrocarbon solvent, such as hexane, benzene, or xylene.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103 in view of Effenberger and Kawabe.

Finally, the Examiner rejected claim 19 under 35 U.S.C. § 103 as allegedly being unpatentable over Fiedge et al. (U.S. 4,218,380). *See Action* at page 7. Applicants respectfully traverse this rejection. The Examiner acknowledged that Fiedge does not describe a packing density. The Examiner went on to describe packing density as "not related to the novelty of the instant invention, but rather is naturally obtained as a unique physical property for evaluating the compound." *Id.* Applicants respectfully traverse. As indicated in the specification, the packing density of a crystal can be affected by the method used to produce that crystal. *See Specification* at page 46. Indeed, according to the specification, optically active chloromandelic acid produced

using certain methods of the instant invention has a packing density greater than 0.5, while "the packing density of the same crystal obtained by the previous methods is less than 0.50." *Id.* The Examiner has not explained how Fiedge renders obvious an optically active chloromandelic acid with a packing density greater than 0.50. Accordingly, Applicants respectfully request withdrawal of the rejection of claim 19 under § 103 in view of Fiedge.

CONCLUSION


Applicants respectfully assert that the present application is in condition for allowance and request that the Examiner issue a timely Notice of Allowance for pending claims 1-3, 7-9, 11, and 13-19.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: August 12, 2003

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INTRODUCTION TO INSTRUMENTAL ANALYSIS

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New York St. Louis San Francisco Auckland Bogotá Hamburg
Johannesburg London Madrid Mexico Milan Montreal New Delhi
Panama Paris São Paulo Singapore Sydney Tokyo Toronto

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1234567890 DOCDOC 89876

ISBN 0-07-007291-4

This book was set in Times Roman by Santype International Limited.
The editor was Karen S. Misler; the production supervisor
was Leroy A. Young; the cover was designed by John Hite.
Project supervision was done by Santype International Limited.
R. R. Donnelley & Sons Company was printer and binder.

Library of Congress Cataloging-in-Publication Data

Braun, Robert D.
Introduction to instrumental analysis.

Includes bibliographical references.

1. Instrumental analysis. I. Title.

QD79.15B73 1987 543'.08 86-30
ISBN 0-07-007291-4

LIQUID CHROMATOGRAPHY

Liquid chromatography (LC) is the general name for the several types of chromatography which use a liquid mobile phase. Several categories of liquid chromatography are used. *Liquid-solid chromatography* (LSC) uses a liquid mobile phase and a solid stationary phase. The rate at which a chemical species travels through an LSC column is determined by the amount of time that the species spends adsorbed on the surface of the solid stationary phase. As the time of adsorption increases, the retention time also increases. Because LSC depends upon adsorption to the stationary phase, the technique is sometimes termed *adsorption chromatography*.

Liquid-liquid chromatography (LLC) uses immiscible liquids for the stationary and mobile phases. The stationary-phase liquid is held in place either as a coating on solid particles which are packed into the column or as a coating on the interior of the column wall. The rate at which a chemical species travels through an LLC column depends upon the relative solubility of the species in the stationary phase as compared with its solubility in the mobile phase. As the relative solubility in the stationary phase increases, the retention time of the species lengthens. Because separation in LLC depends upon the ability of the mixture components to partition, i.e., divide, themselves between two liquid phases, LLC is sometimes termed *partition chromatography*. The partition coefficient [Eq. (24-1)] is used to quantitatively describe the separation that occurs between the two liquid phases.

Ion-exchange chromatography uses a cation or anion exchanger as the stationary phase. The mobile phase is normally water, although in some circumstances mixtures of water and organic solvents are used. Sample component ions are attracted to exchange sites on the ion exchanger. Separation of the sample into ionic groups is based on the relative attraction of the ion-exchange sites for

the individual ionic types. If an ion is strongly attracted to an ion-exchange site that is already occupied by a weakly attracted ion, the strongly attracted ion displaces the weakly attracted ion. The displacement of one ion on a stationary phase by a second ion is *ion exchange*. As the attraction between an ion and the stationary ion-exchange site increases, the retention time of the ion in the column increases. Ion-exchange chromatography differs from the forms of liquid chromatography described previously in that ions rather than neutral molecules are separated.

A particularly useful form of LC is actually a subdivision of each of the previously described types. By decreasing the particle size of the stationary packing material, the surface area of the stationary phase that is exposed to the mobile phase is increased. The result is a tightly packed column that is more efficient. To achieve the same mobile-phase flowrate through a tightly packed column as through a less tightly packed column, it is necessary to use a higher mobile-phase inlet pressure. The type of liquid chromatography which uses these high-efficiency columns and relatively high mobile-phase inlet pressures is termed either *high-performance liquid chromatography* or *high-pressure liquid chromatography*. Both names are abbreviated to HPLC. HPLC is the most popular form of chromatography that is used for chemical analysis.

Plane chromatography is a form of liquid chromatography in which the stationary phase is held on or in a plane rather than in a column. The plane can be a glass or plastic plate (*thin-layer chromatography*) or a piece of filter paper or cellulose (*paper chromatography*). In either case the mobile phase is a liquid. Separation is caused by adsorption, relative solubility, or both adsorption and relative solubility on or in the stationary phase. In *size-exclusion chromatography* (SEC), a gel is used as the stationary phase. Separation is based on molecular size. In *affinity chromatography* a stationary phase preferentially binds a specific sample component to it chemically. Separation in that case results from the chemical reactivity of the sample components with the stationary phase. In *electrophoresis* charged electrodes aid in the separation. An ion migrates toward the oppositely charged electrode at a rate that is dependent upon the ionic charge and the mobility of the ion in or on the stationary phase. Ions are separated based upon their charge and mobility.

LIQUID-SOLID CHROMATOGRAPHY

The descriptive material in the sections that are devoted to LSC, LLC, and ion-exchange chromatography apply both to traditional and high-performance chromatography. The chromatographic principles that are introduced are identical for traditional and high-performance liquid chromatography. Several later sections in the chapter are devoted exclusively to HPLC. The high-performance methods are generally more useful for chemical analysis than the traditional chromatographic methods.

The assembled apparatus that is used for HPLC is described in a later